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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,197	12/09/2003	Wayne P. Franco	0147-1 DIV2	5356

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EXAMINER	
NICHOLS, CHRISTOPHER J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,197	FRANCO, WAYNE P.	
	Examiner	Art Unit	
	Christopher J Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4.26.04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Preliminary Amendment filed 9 December 2003 has been received and entered in full.

2. The Preliminary Amendment filed 16 September 2004 has been received and entered in full.

Specification

3. The disclosure is objected to because of the following informalities: typos "FGB-2" and "BFGF" (**[00023]**). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims **16, 24,** and **31** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "acute coronary artery disease" but the Examiner failed to find an art-accepted definition for this term in the NIH MeSH National Library of Medicine database, www.dictionary.com, and the University of Newcastle upon Tyne's On-Line Medical Dictionary (see references). Therefore, the Examiner has treated "acute coronary artery disease" as "coronary artery disease", the most relevant and art-accepted term encompassed by the limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim **31** is rejected under 35 U.S.C. 102(a) as being anticipated by Spallarossa *et al.* (15 August 1999) "Evaluation of Growth Hormone Administration in Patients With Chronic Heart Failure Secondary to Coronary Artery Disease." The American Journal of Cardiology **84**(4): 430-433.

6. Spallarossa *et al.* teaches the treatment of patients with coronary artery disease via administration of growth hormone (GH) and monitoring the effects of the potential therapy using echocardiogram measurements to assess the therapy thus meeting the limitations of claim 31 (Figure 1; Table I).

7. Claims **16, 22, 31,** and **35** are rejected under 35 U.S.C. 102(b) as being anticipated by Vassenelli *et al.* (December 1987) "Comparison of Different Pharmacological Interventions on Enzymatic Parameters During Acute Myocardial Infarction." Clinical Biochemistry **20**(6): 441-447.

8. Vassenelli *et al.* teaches the evaluation of several pharmaceutical compositions, antiplatelet drugs, anticoagulants, streptokinase, Ca^{2+}-channel blockers, nitrates, and β-blockers

for treating patients suffering from acute myocardial infarction (AMI) by measuring CK-MB before and after treatment thus meeting the limitations of claims 16, 22, 31, and 35 (Tables 1-3; Figure 4). The Examiner notes that CK-MB and CPK-MB are synonymous in the art (see below).

9. Claims **31, 32,** and **35** are rejected under 35 U.S.C. 102(b) as being anticipated by Sellke *et al.* (June 1998) "Therapeutic Angiogenesis With Basic Fibroblast Growth Factor: Technique and Early Results." Ann Throac Surg **65**(6): 1540-1544.

10. Sellke *et al.* teaches the treatment of patients with coronary artery disease via implantation of heparin-alginate bFGF beads and monitoring the effects of the potential therapy using two clinical indicators: restring thallium (REST TL) and exercise sestamibi (EX MIBI) thus meeting the limitations of claims 31, 32, and 35 (Figures 1-2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims **16-35** are rejected under 35 U.S.C. 103(a) as being unpatentable over Sellke *et al.* (June 1998) "Therapeutic Angiogenesis With Basic Fibroblast Growth Factor: Technique and Early Results." Ann Throac Surg **65**(6): 1540-1544 and US 6,620,784 B1 (16 September 2003) Ferrara & Kuo in view of D'Souza *et al.* (October 1978) "The significance of the MB isoenzyme

in patients with acute cardiovascular disease with a normal or borderline total CPK activity." Clinical Biochemistry **11**(5): 204-209.

12. Sellke *et al.* teaches the treatment of patients with coronary artery disease via administration of bFGF and monitoring the effects of the potential therapy using two clinical indicators: restring thallium (REST TL) and exercise sestamibi (EX MIBI) thus meeting the limitations of claims 18, 31, 32, and 35 (Figures 1-2). However, Sellke *et al.* does not teach the administration of VEGF and/or aFGF or the use of CPK-MB as a clinical indicator.

13. '784 teaches administration of VEGF a growth factor, to treat coronary artery disease including but not limited to reperfusion injury such as restenosis subsequent to balloon angioplasty thus meeting the limitations of claims 17, 19, 22, 23, 24, 26, 29, and 30 (Col. 1, 4-5, 7, 9-10, 13-14, 42, 50). '784 teaches that the pharmaceutical composition comprising VEGF may be a nose spray (an aerosol) or a dry powder thus meeting the limitations of claims 20, 21, 27, 28, 33, 34 (Col. 46-52). '784 teaches that the pharmaceutical composition comprising VEGF may be made and used in combination with other growth factors including but not limited to bFGF and/or aFGF thus meeting the limitations of claims 17, 19, 24, 26, and 32 (Col. 52).

14. D'Souza *et al.* teaches measurement of CPK-MB has remarkable sensitivity and specificity for cardiac myofiber damage making it a highly desirable clinical marker for acute or less severe coronary artery disease such as acute myocardial infarct, acute chest pain (angina), and resulting from coronary bypass surgery thus meeting the limitations of claims 16, 24, and 31 (pp. 207; Tables I-III).

15. It would have been obvious to a person of ordinary skill in the art at the time of the invention to combine the therapies of Sellke *et al.* and '784 with the diagnostic method of

D'Souza *et al.* because both Sellke *et al.* and '784 teach the beneficial effects on coronary artery disease of growth factors such as VEGF, aFGF, and bFGF. In addition, D'Souza *et al.* teaches that CPK-MB has remarkable sensitivity and specificity for cardiac myofiber damage making it a highly desirable clinical marker for acute or less severe coronary artery disease such as acute myocardial infarct, acute chest pain (angina), and resulting from coronary bypass surgery.

16. A person of ordinary skill in the art at the time of the invention would be motivated to combine Sellke *et al.* and '784's therapy methods with the diagnostic method of D'Souza because teaches that acute myocardial infarcts are often difficult to diagnosis and CPK-MB measurement overcomes this problem. Further both Sellke *et al.* and '784 teach the beneficial pleiotropic effects of growth factor therapy.

Summary

17. No claims are allowed.

18. The Examiner notes that bFGF is also known as basic FGF and FGF-2 [see Bikfalvi *et al.* (1997) "Biological Roles of Fibroblast Growth Factor-2." Endocrine Reviews **18**(1): 26-45]. The Examiner notes that "CPK-MB" and "CK-MB" are interchangeable abbreviations for "creatine phosphokinase myocardial isoform" in the art [see Sato *et al.* (1997) "Hepatocyte growth factor (HGF): a new biochemical marker for acute myocardial infarction." Heart Vessels **12**(5): 241-6 and US 5,817,640 (6 October 1998) Gruber *et al.*]

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

CJN
October 19, 2004

Elizabeth C. Hemmens